# **PCT**

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



| 51) International Patent Classification 6:   |  | (11) International Publication Number: WO 99/6546  |
|--|--|--|
| A61K 9/16, 9/51, 9/14  | A3   | (43) International Publication Date: 23 December 1999 (23.12.9   |
| <ul> <li>21) International Application Number: PCT/U</li> <li>22) International Filing Date: 18 June 1999</li> <li>30) Priority Data: 60/089,852 19 June 1998 (19.06.98)</li> <li>71) Applicant: RTP PHARMA INC. [CA/US]; 4364 Sc Avenue, Durham, NC 27713–2280 (US).</li> <li>72) Inventors: PACE, Gary, W.; 6913 Hunters Way NC 27615 (US). VACHON, G., Michael; Strathcona, Westmount, Quebec H3Y 2X2 (CA). K., Awadhesh; Appartement 201, 670 de Gasp Soeurs, Verdun, Quebec H3E 1H8 (CA). HE Inge, B.; Lagaardsvegen 131, N–4010 Stavat KRUKONIS, Val; 287 Emersion Road, Lexit 02173 (US). GODINAS, Anthony; 30 Washing Methuen, MA 01844 (US).</li> <li>74) Agent: CRAWFORD, Arthur, R.; Nixon &amp; Vanderhy floor, 1100 North Glebe Road, Arlington, VA 2</li> </ul>  | y, Raleig<br>445, n<br>MISHR.<br>be, Iles d<br>NRIKSEI<br>nger (NC<br>ngton, M<br>gton Stree | (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, B BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, G GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, IP, KE, K KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, M MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, S SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZV ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, U ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, T TM), European patent (AT, BE, CH, CY, DE, DK, ES, I FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI pate (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, N SN, TD, TG).  Published With international search report. Before the expiration of the time limit for amending the clair and to be republished in the event of the receipt of amendmen  (88) Date of publication of the international search report: 2 March 2000 (02.03.0)   |
| (US).  |  |  |
| uspensions of same with surface modifier molecules to<br>ompound and surface modifiers in a liquefied gas and co   | is, particu  | larly drugs, are prepared by simultaneously stabilizing microparticular<br>expansion into an aqueous medium from a compressed solution of t  |
| 57) Abstract  Submicron particles of water-insoluble compound uspensions of same with surface modifier molecules by  | is, particu  | larly drugs, are prepared by simultaneously stabilizing microparticul expansion into an aqueous medium from a compressed solution of   |
| Submicron particles of water-insoluble compound uspensions of same with surface modifier molecules to ompound and surface modifiers in a liquefied gas and of the surface modi | is, particu  | larly drugs, are prepared by simultaneously stabilizing microparticul expansion into an aqueous medium from a compressed solution of   |
| Submicron particles of water-insoluble compound uspensions of same with surface modifier molecules to ompound and surface modifiers in a liquefied gas and of the surface modi | is, particu  | larly drugs, are prepared by simultaneously stabilizing microparticul expansion into an aqueous medium from a compressed solution of   |
| Submicron particles of water-insoluble compound uspensions of same with surface modifier molecules to ompound and surface modifiers in a liquefied gas and of the surface modi | is, particu  | Icles of water-insoluble compounds  larly drugs, are prepared by simultaneously stabilizing microparticular expansion into an aqueous medium from a compressed solution of the compound of the expansion of the ex |

#### FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

| AL | Albania                  | ES | Spain               | LS  | Lesotho               | SI | Slovenia                 |
|----|--------------------------|----|---------------------|-----|-----------------------|----|--------------------------|
| AM | Armenia                  | FI | Finland             | LT  | Lithuania             | SK | Slovakia                 |
| AT | Austria                  | FR | France              | LU  | Luxembourg            | SN | Senegai                  |
| AU | Australia                | GA | Gabon               | LV  | Latvia                | SZ | Swaziland                |
| AZ | Azerbaijan               | GB | United Kingdom      | MC  | Monaco                | TD | Chad                     |
| BA | Bosnia and Herzegovina   | GE | Georgia             | MD  | Republic of Moldova   | TG | Togo                     |
| BB | Barbados                 | GH | Ghana               | MG  | Madagascar            | TJ | Tajikistan               |
| BE | Belgium                  | GN | Guinea              | MK  | The former Yugoslav   | TM | Turkmenistan             |
| BF | Burkina Faso             | GR | Greece              |     | Republic of Macedonia | TR | Turkey                   |
| BG | Bulgaria                 | HU | Hungary             | ML  | Mali                  | TT | Trinidad and Tobago      |
| BJ | Benin                    | IE | Ireland             | MN  | Mongolia              | UA | Ukraine                  |
| BR | Brazil                   | ΙL | Israel              | MR  | Mauritania            | UG | Uganda                   |
| BY | Belarus                  | IS | Iceland             | MW  | Malawi                | US | United States of America |
| CA | Canada                   | IT | Italy               | MX  | Mexico                | UZ | Uzbekistan               |
| CF | Central African Republic | JP | Japan               | NE  | Niger                 | VN | Vict Nam                 |
| CG | Congo                    | KE | Kenya               | NL  | Netherlands           | YU | Yugoslavia               |
| CH | Switzerland              | KG | Kyrgyzstan          | NO  | Norway                | zw | Zimbabwe                 |
| CI | Côte d'Ivoire            | KP | Democratic People's | NZ  | New Zealand           |    |                          |
| CM | Cameroon                 | *  | Republic of Korea   | PL, | Poland                |    |                          |
| CN | China                    | KR | Republic of Korea   | PT  | Portugal              |    |                          |
| CU | Cuba                     | KZ | Kazakstan           | RO  | Romania               |    |                          |
| CZ | Czech Republic           | LC | Saint Lucia         | RU  | Russian Federation    |    |                          |
| DE | Germany                  | LI | Liechtenstein       | SD  | Sudan                 |    |                          |
| DK | Denmark                  | LK | Sri Lanka           | SE  | Sweden                |    |                          |
| EE | Estonia                  | LR | Liberia             | SG  | Singapore             |    |                          |

### INTERNATIONAL SEARCH REPORT

Inte onal Application No PCT/US 99/13755

| A CLASS        | IEICATION OF CUR IECT MATTER  |   |   |
|----------------|---|---|---|
| ÎPC 6          | FICATION OF SUBJECT MATTER A61K9/16 A61K9/51 A61K9/1  | 4   |   |
|                |   |   |   |
|                | o International Patent Classification (IPC) or to both national classific   | eation and IPC  |   |
|                | SEARCHED  ocumentation searched (classification system followed by classification)                                  | in a combata  |   |
| IPC 6          | A61K  | ion symbols)  |   |
| Documenta      | tion searched other than minimum documentation to the extent that   | such documents are each aled in the fields as   | ansahad                                       |
| Documenta      | Source of the than minimum documentation to the extent that   | such documents are included in the helps se   | sarched                                       |
| Claster sia e  |   |   |   |
| Electionic d   | late base consulted during the international search (name of data be  | ase and, where practical, search terms used   | 1   |
|                |   |   |   |
|                |   |   |   |
|                |   | ·   |   |
|                | ENTS CONSIDERED TO BE RELEVANT  | · · · · · · · · · · · · · · · · · · ·   |   |
| Category *     | Citation of document, with indication, where appropriate, of the re   | levant passages   | Relevant to claim No.                         |
| Ε              | WO 99 52504 A (HOFFMANN LA ROCHE  | \   | 1-16  |
| _              | 21 October 1999 (1999-10-21)  | ,   | 1-10  |
|                | the whole document  |   |   |
| Α              | WO 97 14407 A (RES TRIANGLE   |   | 1-16  |
|                | PHARMACEUTICALS ;UNIV TEXAS (US)  | ;   |   |
|                | HENRIKSEN INGE B (U)  |   |   |
|                | 24 April 1997 (1997-04-24)<br>cited in the application  |   |   |
|                | the whole document  |   |   |
| A              | <br>WO 95 21688 A (WEIDNER ECKHARD ;  | VNE7  |   |
| ^              | ZELJKO (SI); NOVAK ZORAN (SI))  | NNEZ  |   |
|                | 17 August 1995 (1995-08-17)   |   | •   |
| Α              | US 3 998 753 A (ANTOSHKIW THOMAS  | WTHITAM   |   |
| ,,             | ET AL) 21 December 1976 (1976-12  |   |   |
|                |   | ,   |   |
|                |   | -/ <b></b>  |   |
| [V] 5          | I her documents are listed in the continuation of box C.  | N Octobrit manhor on field  | in annu                                       |
| <u> </u>       | ner documents are asted in the Continuation of box C.   | Patent family members are listed  | m annex.                                      |
|                | stegories of cited documents :  | "T" (ater document published after the inte<br>or priority date and not in conflict with  | mational filing date                          |
|                | ent defining the general state of the art which is not<br>tered to be of particular relevance                       | cited to understand the principle or the invention  |   |
| "E" earlier of | document but published on or after the international tate   | "X" document of particular relevance; the c cannot be considered novel or cannot  |   |
| which          | ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another            | involve an inventive step when the do- "Y" document of particular relevance; the c  | cument is taken alone                         |
| O docume       | n or other special reason (as specified)<br>ent referring to an oral disclosure, use, exhibition or                 | cannot be considered to involve an involve an involve and involve | ventive step when the<br>are other such docu- |
|                | means ent published prior to the international filing date but  | ments, such combination being obvious<br>in the art.  | us to a person skilled                        |
| later th       | han the priority date claimed   | "&" document member of the same patent  |   |
| Date of the    | actual completion of the international search   | Date of mailing of the international sea  | arch report                                   |
| 2              | 3 December 1999   | 12/01/2000  |   |
| Name and r     | mailing address of the ISA<br>European Patent Office, P.B. 5818 Patentlaan 2  | Authorized officer  |   |
|                | Purpean Patent Unice, P.B. 5616 Patentiaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, | <b>.</b>  |   |
|                | Fax: (+31-70) 340-2040, 1x: 31 651 690 hi,  | Fischer, W  |   |

2

## INTERNATIONAL SEARCH REPORT

Int: .ional Application No PCT/US 99/13755

| .(Continual | ion) DOCUMENTS CONSIDERED TO BE RELEVANT  | PC1/03 99 |                       |
|-------------|---|-----------|-----------------------|
|             | Citation of document, with indication,where appropriate, of the relevant passages |           | Relevant to claim No. |
|             | G. DONSI ET AL.: "POSSIBILITY OF APPLICATION TO PHARMACEUTICAL FIELD"             | <u> </u>  |                       |
|             | PHARM. ACTA HELV,1991 - 1991, pages 170-173, XP002900588                          |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           | , ·                   |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           | ·                     |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |
|             |   |           |                       |

## INTERNATIONAL SEARCH REPORT

.aformation on patent family members

Inte ional Application No PCT/US 99/13755

|    | atent document<br>d in search repor | t | Publication date |  | Patent family<br>member(s)   | Publication date   |
|----|-------------------------------------|---|------------------|--|--|--|
| WO | 9952504                             | Α | 21-10-1999       | NONE   |  |  |
| WO | 9714407                             | A | 24-04-1997       | AU<br>AU<br>EP                                     | 709262 B<br>7461796 A<br>0855906 A   | 26-08-1999<br>07-05-1997<br>05-08-1998   |
| WO | 9521688                             | A | 17-08-1995       | SI<br>AT<br>CA<br>DE<br>DK<br>EP<br>ES<br>GR<br>JP | 9400079 A<br>159184 T<br>2182786 A<br>59500808 D<br>744992 T<br>0744992 A<br>2109095 T<br>3025495 T<br>9508851 T | 31-10-1995<br>15-11-1997<br>17-08-1995<br>20-11-1997<br>02-06-1998<br>04-12-1996<br>01-01-1998<br>27-02-1998<br>09-09-1997 |
| US | 3998753                             | A | 21-12-1976       | AT<br>AT<br>BE<br>DE<br>FR<br>GB<br>IT<br>JP<br>NL | 351912 B<br>625675 A<br>832331 A<br>2534091 A<br>2281961 A<br>1502895 A<br>1050722 B<br>51041732 A<br>7509586 A  | 27-08-1979<br>15-01-1979<br>12-02-1976<br>26-02-1976<br>12-03-1976<br>08-03-1978<br>20-03-1981<br>08-04-1976<br>17-02-1976 |